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REMARKS

Applicants wish to thank the Examiner for the telephonic interview of December 4, 2007. Applicants have amended independent claims 27 and 48. Dependent claim 32, which was not discussed during the interview, has been amended for reasons related to clarity. Although the amendments to independent claims 27 and 48 are not exactly those discussed during the telephonic interview, Applicants believe that the current amendments remove unnecessary verbiage and clarify the claimed subject matter in the same manner discussed during the telephonic interview. Applicants request that the Examiner contact the undersigned to discuss the amendments should there be any questions regarding the changes. Applicants also provide the following additional remarks to explain how the subject matter of present claims 27, 30-33, 44, and 47-49 can be distinguished from the subject matter disclosed in the publications cited in the present rejection under 35 U.S.C. § 103(a).

Applicants have amended claims 27 and 48 to clarify that the recited methods involve the *in vitro* detection of a given, predefined pathological condition that causes disease in a tissue distinct from blood cells by detecting hybridization between 1) a plurality of nucleic acid molecules from a subject being tested for the pathological condition and 2) nucleic acid molecules present in a nucleic acid library that are specific for differentially spliced RNAs that are expressed in blood cells from human subjects known to have the pathological condition and that are characteristic of the pathological condition to be detected. The present amendment to independent claims 27 and 48 clarifies that hybridization between the plurality of nucleic acid molecules from the blood cells of the patient to be tested and the nucleic acid molecules of the nucleic acid library, which are specific for differentially spliced RNAs expressed in blood cells from patients known to have the pathological condition, indicates the presence of the pathological condition in the subject.

In contrast to the methods of present independent claims 27 and 48, and claims dependent therefrom, Varesco et al. (Hum. Genet. 93:281-286, 1994) describes the detection of an abnormal mRNA transcript that results from a genetic mutation that is present in the genome of every cell of the patient. Expression of the abnormal mRNA transcript results in the development of

colorectal adenomatous polyps. Mutations in the APC gene are also known to cause disease in blood cells (see, e.g., Wada et al., J Mol Med., 75:139-44, 1997; a copy of the abstract is provided). Thus, Varesco fails to teach or suggest a method for detecting a pathological condition of a tissue distinct from blood cells by using nucleic acid molecules obtained from blood cells.

Morris et al. (U.S. Patent No. 5,770,421) fails to remedy the deficiencies of Varesco. Morris merely discloses the detection of an abnormal genetic translocation, which results in the fusion of the NPM gene with the anaplastic lymphoma kinase (ALK) gene (see col. 1, lines 21-29); Morris clearly fails to teach or suggest the detection of differential splicing events. In any event, the translocation described in Morris causes disease in blood cells (i.e., lymphoma). Thus, Morris, like Varesco, fails to teach or suggest a method for detecting a pathological condition of a tissue distinct from blood cells by using nucleic acid molecules obtained from blood cells.

Applicants submit that the present rejection of claims 27, 30-33, 44, and 47-49 under 35 U.S.C. § 103(a) over Varesco in combination with Morris can be withdrawn. Applicants believe that the present amendment to claims 27, 32, and 48 can be incorporated into the claims as an Examiner's amendment and, once amended, claims 27, 30-33, 44, and 47-49 will be in condition for allowance. Applicants respectfully request that the Examiner contact the undersigned should there be any remaining issues that require resolution.

Respectfully submitted,

Date:_____

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